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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,749	12/23/1999	JENNIFER L. HILLMAN'	PF-0519-1DIV	7908

22428 7590 12/15/2004

FOLEY AND LARDNER  
SUITE 500  
3000 K STREET NW  
WASHINGTON, DC 20007

EXAMINER
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HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/471,749	<b>Applicant(s)</b> HILLMAN ET AL.	
	<b>Examiner</b> Alana M. Harris, Ph.D.	<b>Art Unit</b> 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 21,22,24,27-30,41 and 42 is/are pending in the application.
- 4a) Of the above claim(s) 24, 29, 30, 41 and 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21,22,27 and 28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Request for Continued Examination*

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 12, 2004 has been entered.

2. Claims 21, 22, 24, 27-30, 41 and 42 are pending.

Claims 21 and 28 have been amended.

Claim 25 and 43-45 have been cancelled.

Claims 24, 29, 30, 41 and 42, drawn to non-elected inventions are withdrawn from examination.

Claims 21, 22, 27 and 28 are examined on the merits.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. In anticipation of the instant rejection Applicants' argue that the specification at page 19 identifies the location of phosphorylation sites and a region of SEQ ID NO: 3 that has been identified in various libraries, many of which are associated with

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proliferating or cancerous tissue or an immune response, see Remarks submitted October 12, 2004, pages 6 and 7. Applicants aver "[a] person of ordinary skill in the art would know to maintain these regions in order to maintain the necessary activity and function." These arguments and points of view have been carefully considered, but found unpersuasive.

Claim 21 is broadly drawn to an isolated polypeptide fragment comprising at least 30 contiguous amino acid residues of SEQ ID NO: 3 having apoptotic activity, as well as an immunogenic fragment of SEQ. ID. NO:3 of at least 30 contiguous amino acid residues. Furthermore, the claim is drawn to a polypeptide having at least 95% sequence identity to SEQ ID NO: 3 also having apoptotic activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Nor does the specification provide enablement for variants that have at least 95% sequence identity. Since the amino acid sequence of a protein determines its structural and functional properties, knowledge of which sequences of the amino acids would retain similar biological activity and immunogenicity the same as Applicants' is required. And while Applicants assert "a polypeptide comprising a sequence having at least 95% sequence identity SEQ ID NO: 3, would have up to only 12 amino acid variations as compared to SEQ ID NO: 3" Applicants' specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. Likewise, there is no guidance as to select any particular 30 contiguous amino acid residues of a polypeptide or which 30

amino acid residues of a fragment or polypeptide would retain apoptotic activity or how to implement a fragment in assays to exhibit apoptotic activity. The specification is silent as to how to make sequences with 95% shared identity and capable of retaining apoptotic function. As set forth by Lazar et al. (Molecular and Cellular Biology 8(3): 1247-1252, March 1988), which was provided previously the data wherein substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein. Notwithstanding, changes of 5% of a sequence will inevitably yield products that will not have the same structural characteristics or function as the native sequence.

The disclosure does not provide any information disclosing what fragments of SEQ ID NO:3 should be immunogenic or what sequences in the native amino acid sequences can be mutated/changed to yield a 95% variant with apoptotic activity. The specification exemplifies no examples of the effective use of the sequences consisting of SEQ ID NO:3, nor fragments and variants of these polypeptides as a pharmacological agent, applicability to diagnostic assays or drug discovery. The scope of the claims must bear a reasonable correlation with the scope of enablement. In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to using the myriad of contiguous amino acid residues and variants encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

5. Claims 21, 22, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In anticipation of the instant rejection Applicants argue that the claims have been amended to recite functional language and structure is also provided for the claimed invention. These points of view have been carefully considered, but found unpersuasive.

Claim 21 is broadly drawn to an isolated polypeptide fragment comprising at least 30 contiguous amino acid residues of SEQ ID NO: 3 having apoptotic activity, as well as an immunogenic fragment of SEQ. ID. NO:3 of at least 30 contiguous amino acid residues. Furthermore, the claim is drawn to a polypeptide having at least 95% sequence identity to SEQ ID NO: 3 also having apoptotic activity. The written description in this instant case only sets forth SEQ ID NO:3 consisting of 238 amino acids, therefore the written description is not commensurate in scope with the claims drawn to amino acid sequences sharing 95% sequence identity and a polypeptide comprising a fragment of at least 30 contiguous amino acid residues of a polypeptide of SEQ ID NO: 3.

Remiss from Applicants' disclosure is evidence supporting Applicants' possession of a representative number of species within the claimed genus of polypeptides. Applicants' specification does not evidence undefined and uncharacterized polypeptide fragments comprising at least 30 contiguous amino acid

residues of SEQ ID NO: 3. Applicants' specification also does not provide support for polypeptides comprising a sequence having at least 95% sequence identity to SEQ ID NO: 3. Applicants' citation of function and structure within the claims does not preclude the application of the instant rejection. Assigning the claimed polypeptides with function and structure is not commensurate with evidence of possession of the claimed genus.

*Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:3, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d1016.

Furthermore, In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

There is no disclosure suggesting Applicants were in possession of sequence variants sharing 95% sequence identity with SEQ ID NO: 3 nor polypeptide fragments comprising at least 30 contiguous amino acids residues of SEQ ID NO: 3. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

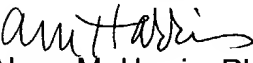
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, but can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**ALANA M. HARRIS, PH.D.**  
**PRIMARY EXAMINER**

  
Alana M. Harris, Ph.D.  
10 December 2004